

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: George P. Lomonosoff *et al.*
Serial No.: 09/304,967
Filed: 05/05/99
Entitled: Modified Plant Viruses As Vectors of Heterologous Peptides
Group No.: 1636
Examiner: D. Guzo

TRANSMITTAL OF FORMAL DRAWINGS

Official Draftsperson
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Dated: May 13, 2004 By: Traci E. Light

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☒ 24 sheets of formal drawing(s) for this application.

☒ Each sheet of drawing indicates the identifying indicia suggested in 37 CFR § 1.84(c) on the front side of the drawing.

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Dated: May 13, 2004

Peter G. Carroll
Registration No. 32,837

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101 Howard Street, Suite 305
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617/984.0616



Serial No.: 09/304,967 Filed: 05/05/99
Examiner: D. Guzo Group Art Unit: 1636
Applicant: George P. Lomonosoff
Title: **Modified Plant Viruses As Vectors
of Heterologous Peptides**
Atty. Docket No.: DOW-04646 Sheet 1 of 24

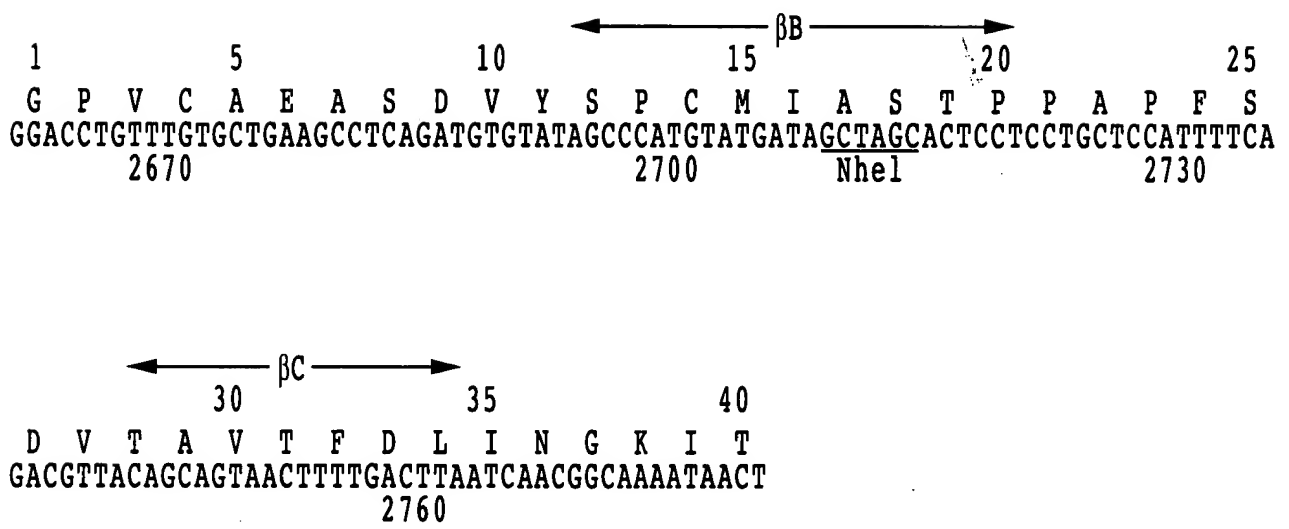


FIG. 1



S T V S R N A V P N L R G D L Q V L A Q K V A R T L P
CTAGCACTATAGTAGAAATGCTGTTCCCTAATTGAGAGGAGATCTTCAAGTTTGGCTCAAAGGTTGCTCGGACTCTTC
GTGAATATCATCTTTACGACAAGGATTAAACTCTCTCTAGAGATTCAAACCGAGTTTCCCAACGAGCCTGAGAAGGATC
BgIII

FIG. 2A

1 5 10 15
G P V C A E A S D V Y S P C M I A S T Y S R N A V P N
GGACCTGTTTGTGCTGAAGCCTCAGATGCTGTATAGCCCATGTATGATAGTAGCCTTATAGTAGAAATGCTGTTCCCTAAT
2670 2700 NheI

20 25
L R G D L Q V L A Q K V A R T L P S T P P A P F S
TTGAGAGGAGATCTTCAAGTTTGGCTCAAAGGTTGCTCGGACTCTTCCCTAGCAGCTCCTCTGCTCCATTTCATCA
BgIII xNheI 2730

FIG. 2B

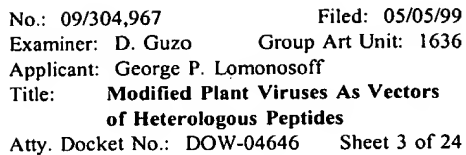


FIG. 3



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15 20 25 30 35
P C M I A S T P P A P F S D V T A V T F D L I
CCATGTATGATAGCTAGCACTCCCTCGCTCCATTTCAGACGTTACAGCAGTAACCTTTTGACTTAATC
2700 NheI 2730 * 2760

△ SITE-DIRECTED MUTAGENESIS

15 20 25 30 35
P C M I A S T P P A P F S D V T A V T F D L I
CCATGTATGATAGCTAGCACTCCCTCGCTCCATTTCAGACGTTACAGCAGTAACCTTTTGACTTAATC
2700 NheI 2730 AatII 2760

FIG. 4

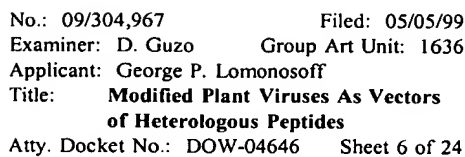


FIG. 6A

↑ 30 H R E A K L D V T A V T F D L I 35
 CATAGAGAAGCTAAATTGGACGTCACAGCAGTAACTTTGGACTTAATC
 AatII 2760

F/G. 6B

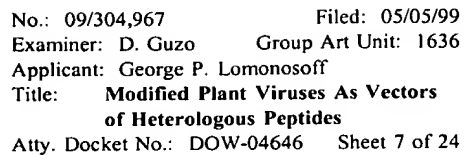
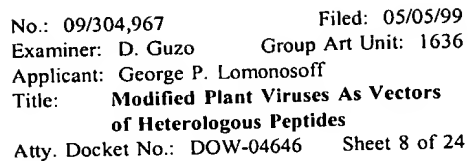


FIG. 7



S T P P A
CTAGCACTCCTCCTGCT
GTCAGGAGGACGA

P P S D
CCATTTCAGACGT
GGTAAAGTC

V P N L R G D L Q V L A Q K V A R T L
G T C C T A A T T T G A G A G G A T C T T C A A G T T T G G C T C A A A G G T T G C T C G G A C T C T T
C A A G G A T T A A A C T C T C C T C T A G A A G T T C A A A C C G A G T T T T C C A A C G A G C C T G A A A

K D A T G I D N H R E A K L
AAAGATGCTACTGGAATCGATAATCATAGAGAACGAAAATTG
TTTCTACGATGACCTTAGCTATTAGTATCTCTCGTTTAAAC

731 P R G P D R P E G I E E E G G E R D R D R S 752
CCTAGAGGACCAGACAGACCTGAGGAATAGAACGAGGAGGATCGAGATAGATCA
GGATCTCCGGTGTCTGGACTTCCTTATCTTCTCCTCCACCTCTTGGCTAGCTCTATAGT

8
G.
F

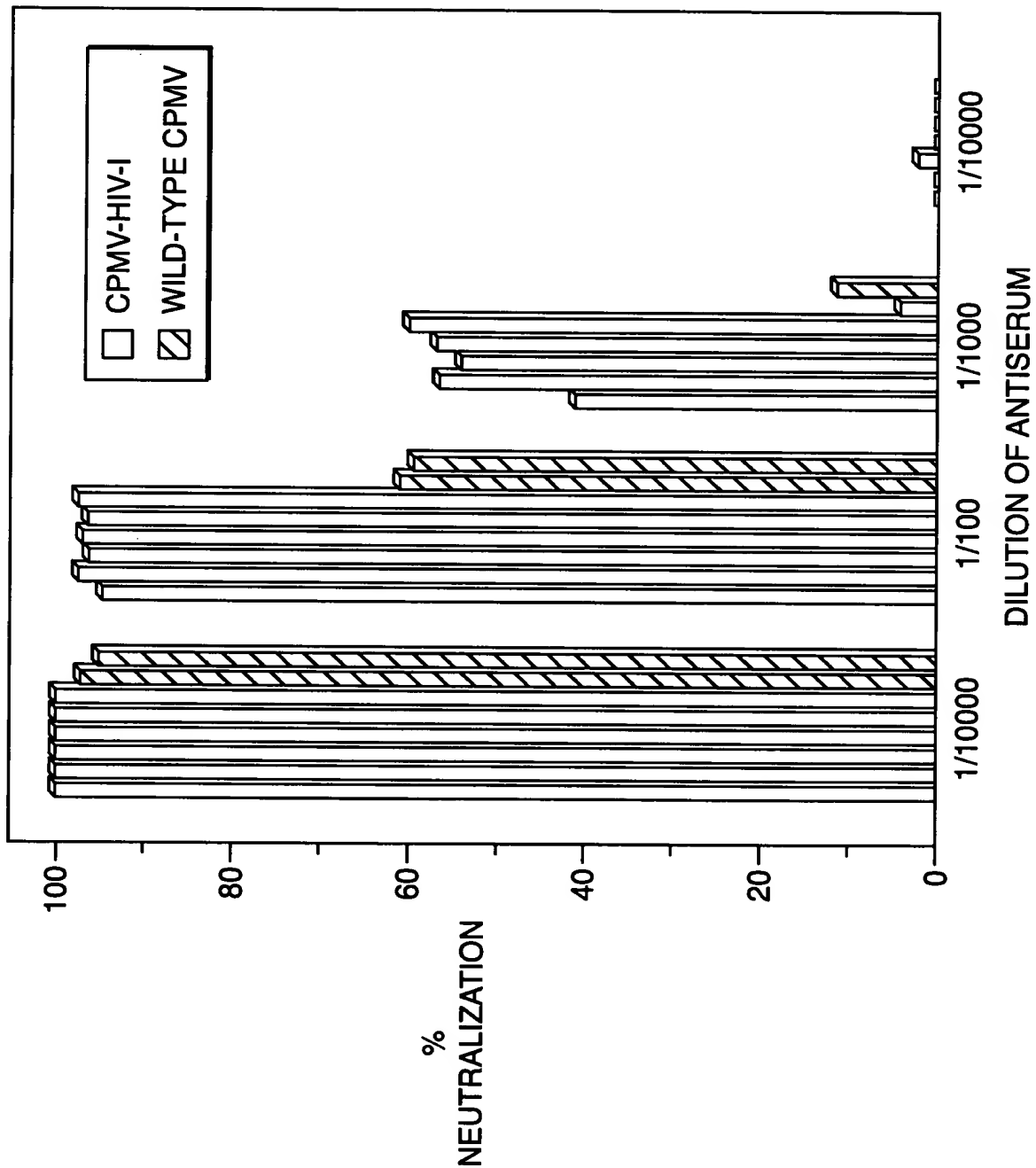


Fig. 9

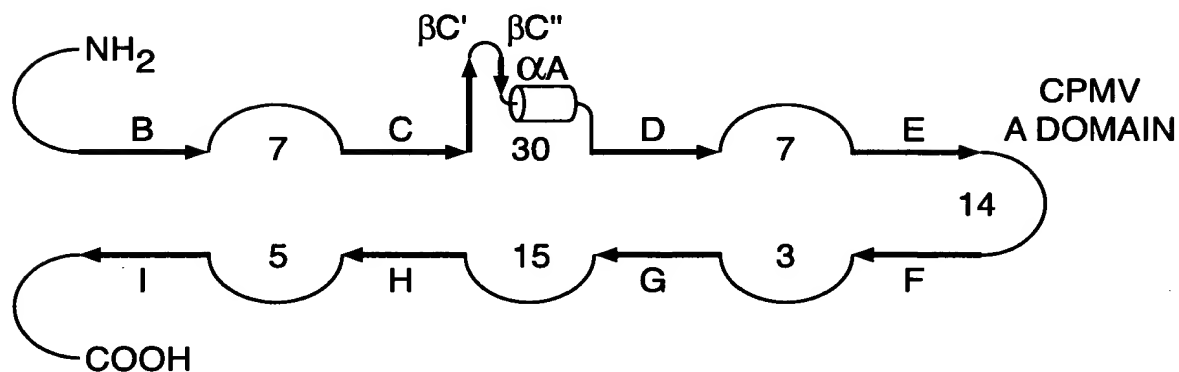
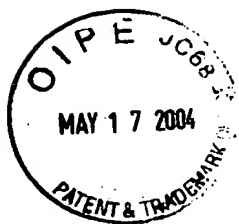


FIG. 10A

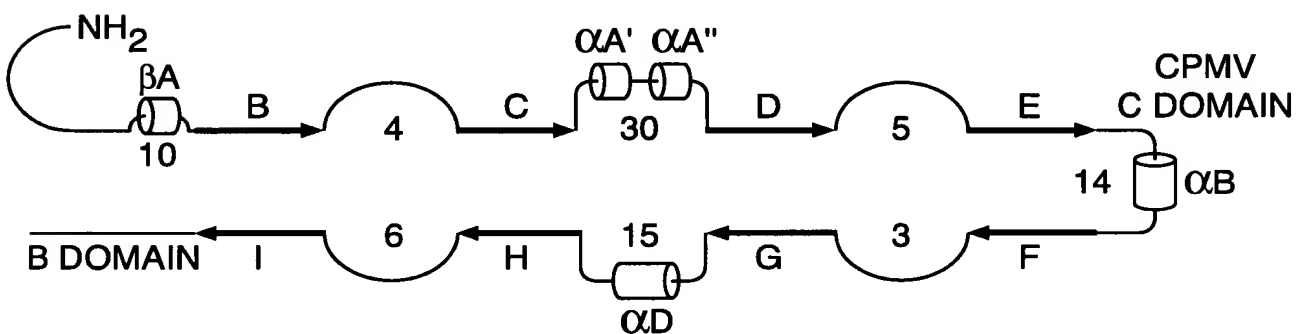


FIG. 10B

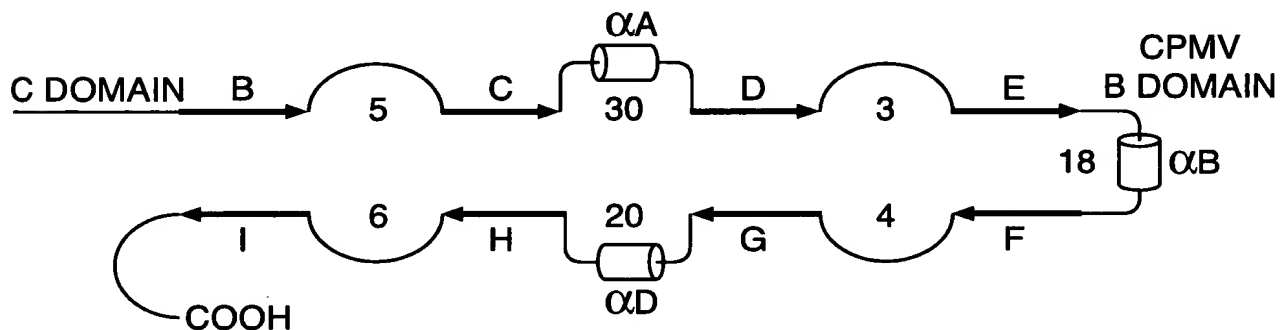


FIG. 10C

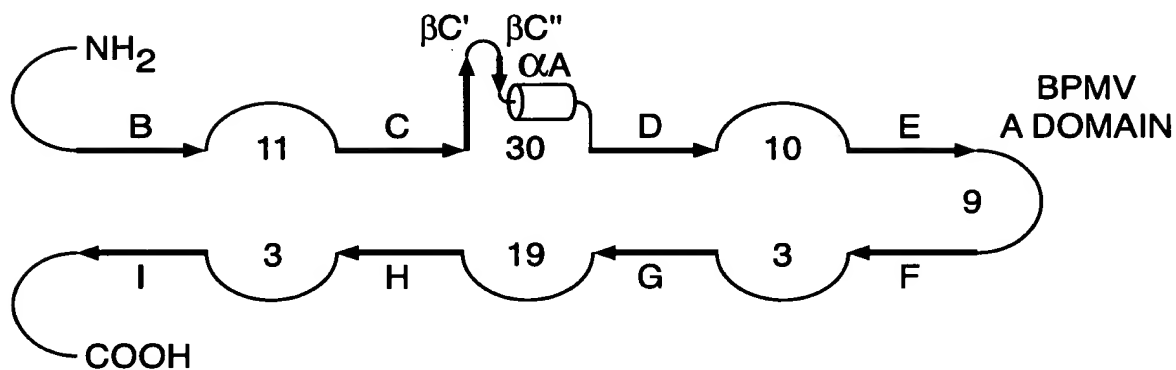
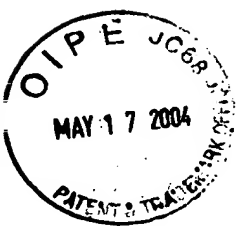


FIG. 10D

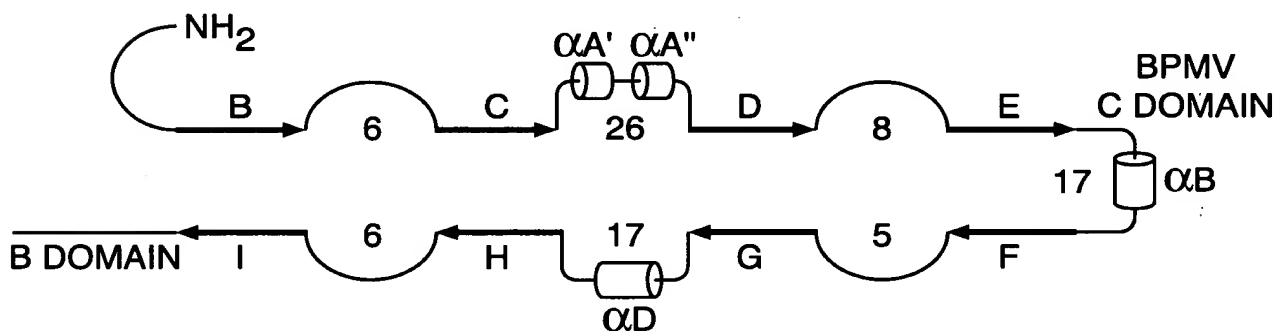


FIG. 10E

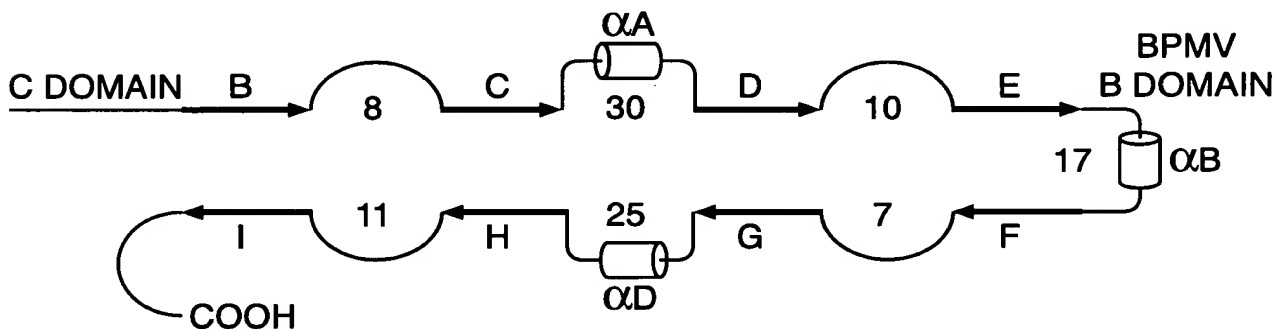


FIG. 10F

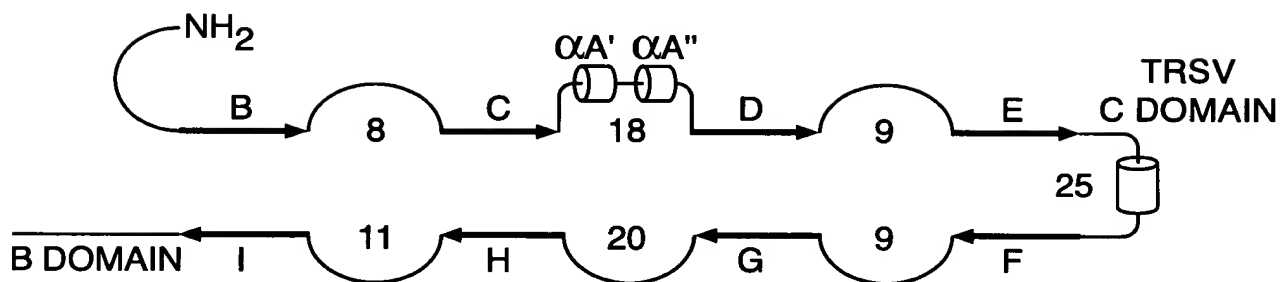
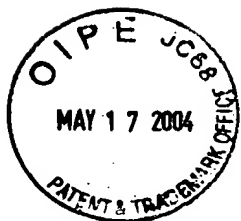


FIG. 10G

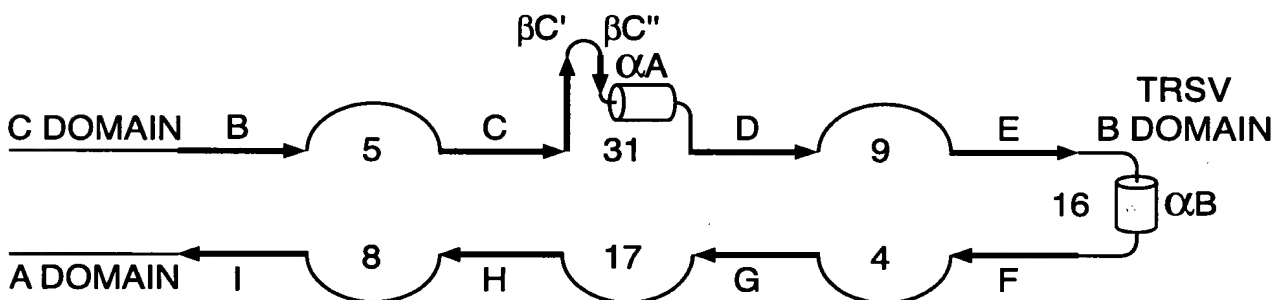


FIG. 10H

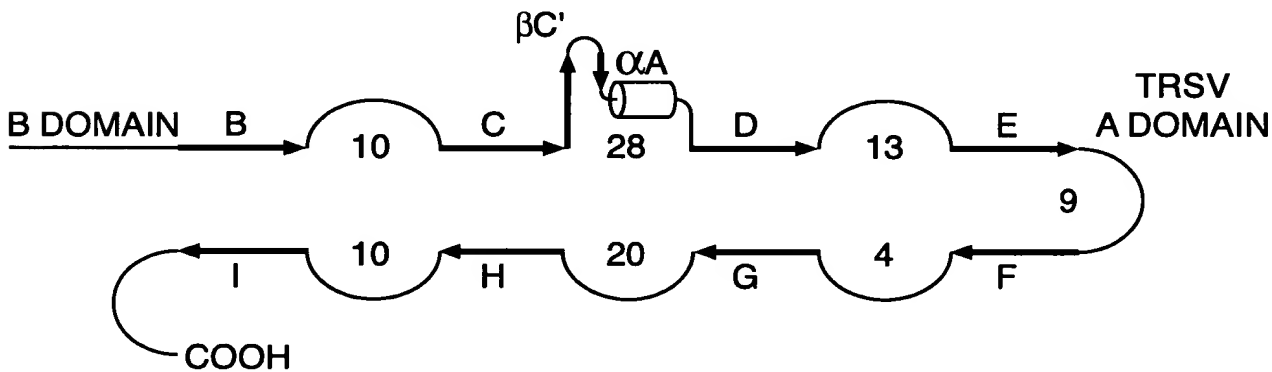


FIG. 10I

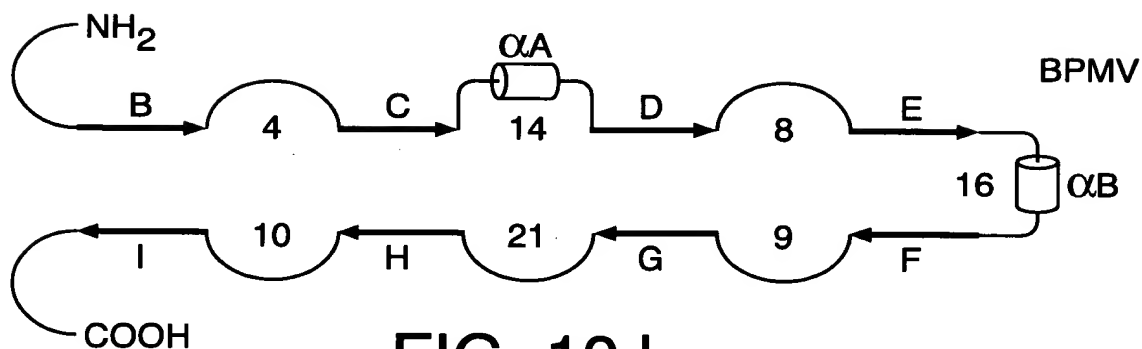


FIG. 10J

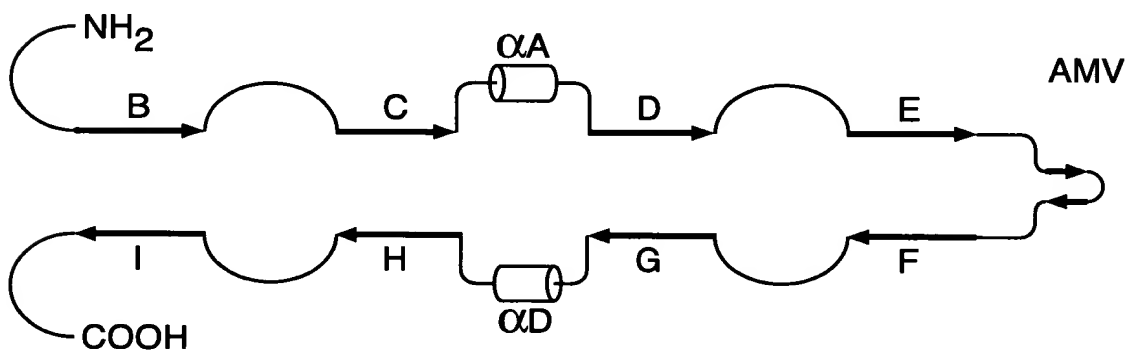


FIG. 10K

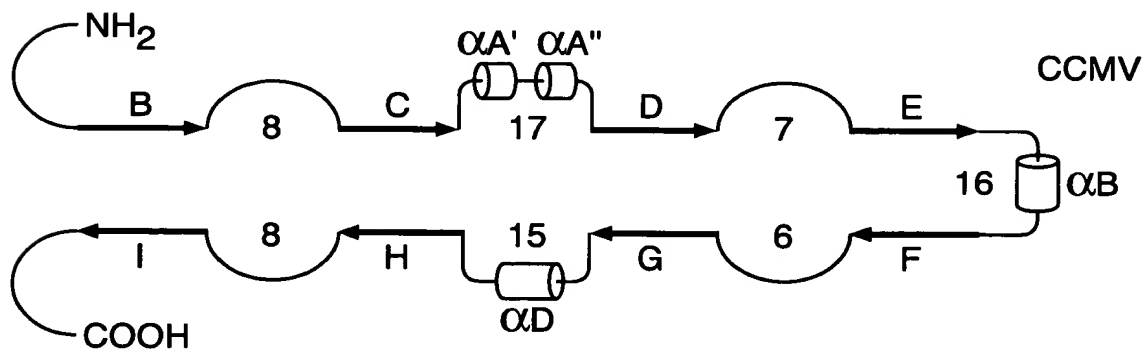


FIG. 10L

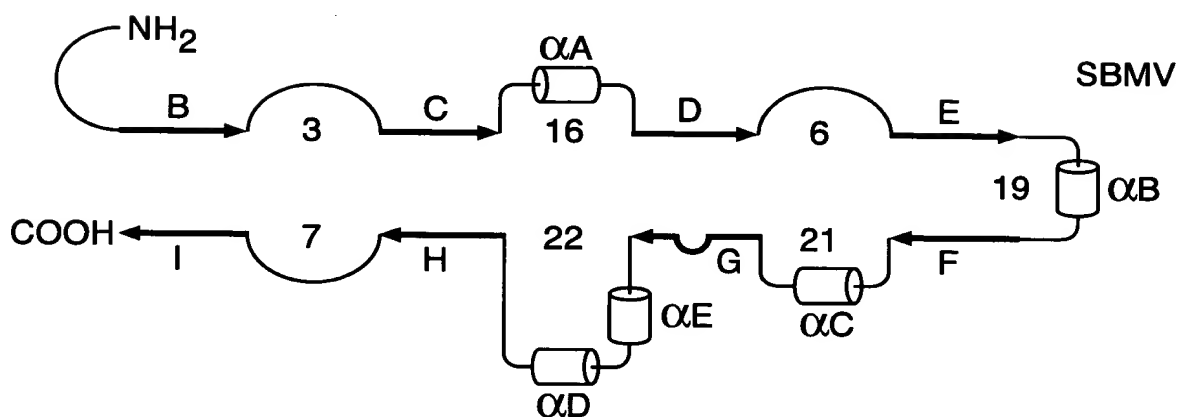


FIG. 10M

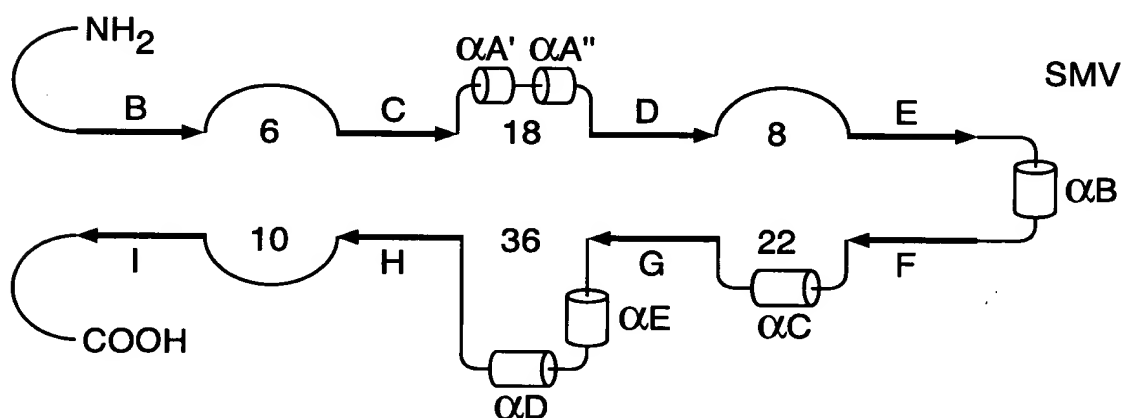


FIG. 10N

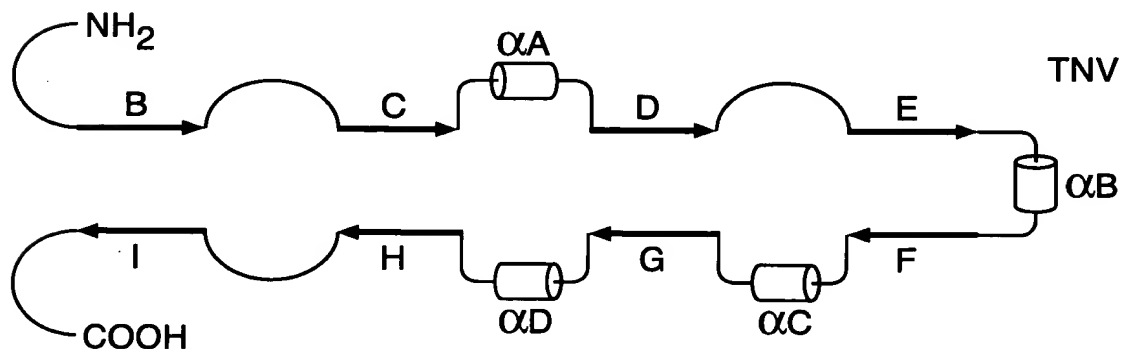


FIG. 10O

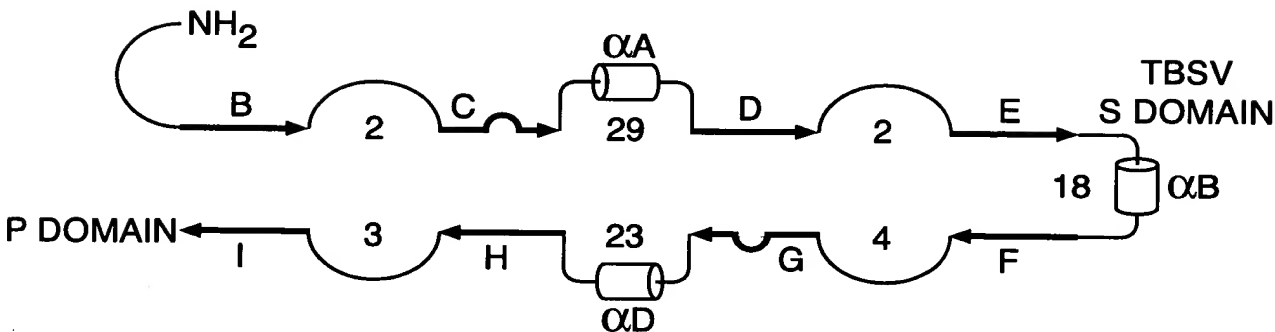
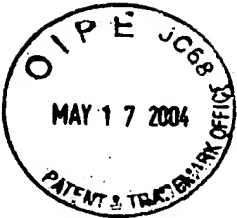


FIG. 10P

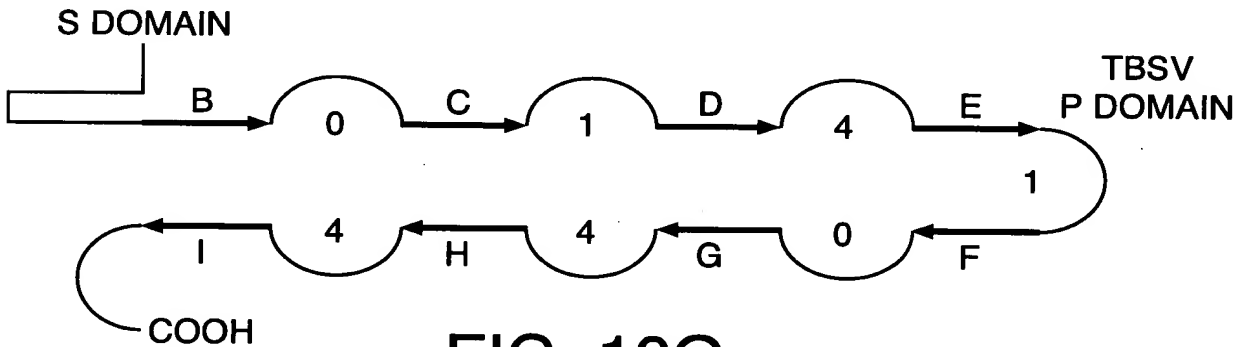


FIG. 10Q

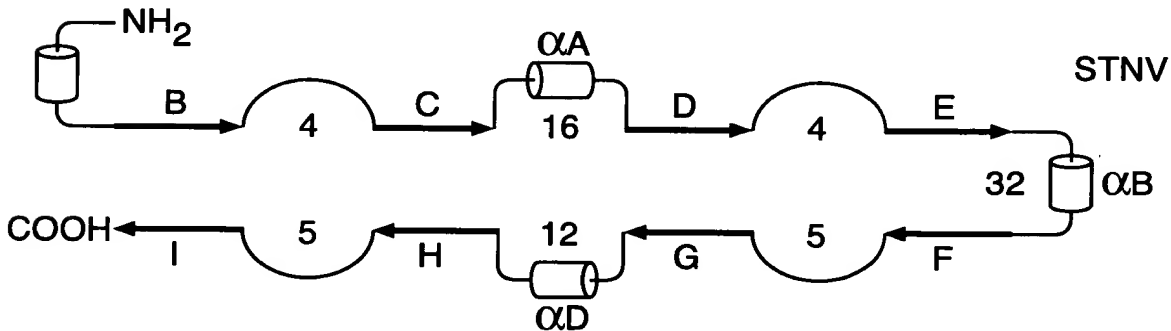


FIG. 10R

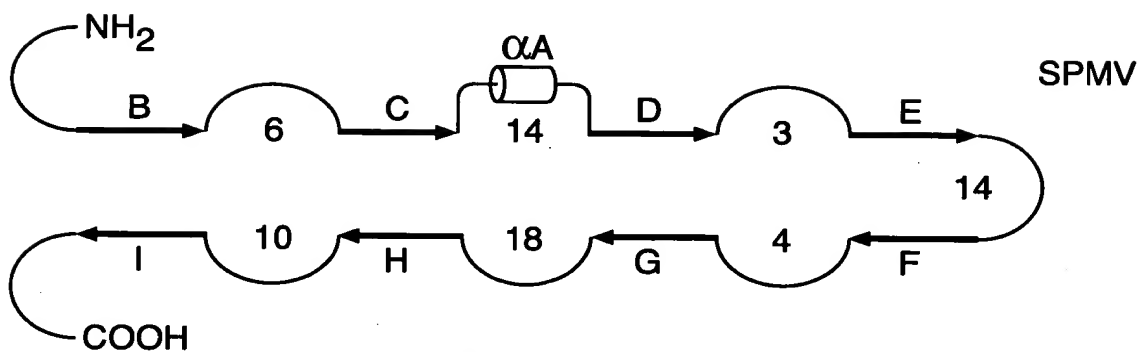
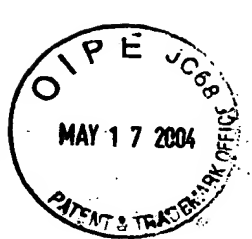


FIG. 10S

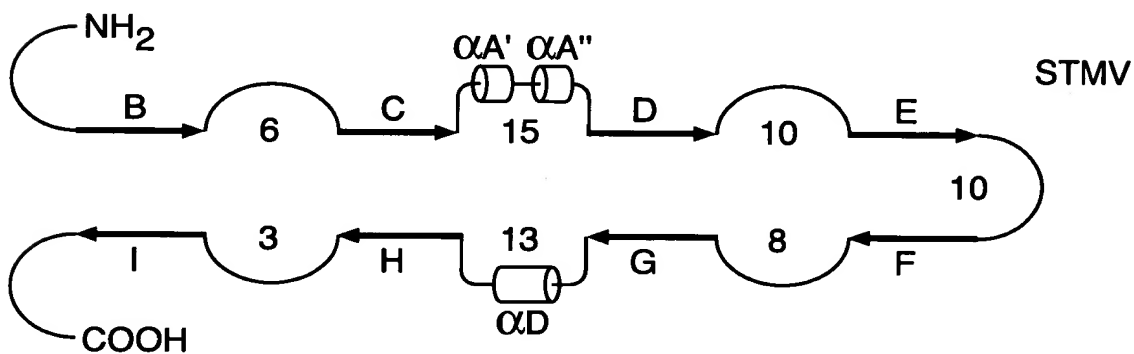
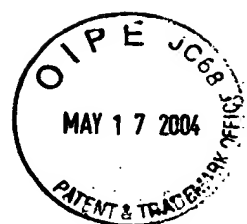


FIG. 10T



SEQUENCE OF SBMV COAT PROTEIN SPANNING THE POTENTIAL INSERTION SITE WITH
INTRODUCED BASE CHANGES AND NEW RESTRICTION SITES: (SEQUENCE STARTS AT nt 3955)

```
      M E G G S S K T A V N T G
      ATGGAAGGAGGATCATCTAAGACTGCTGTGAACACTGGG
              ↓                ↓
          GGATCC          GTTAAC
          BamH I          Hpa I
```

FIG. 11A

SERIES OF SEQUENCES TO BE INSERTED BETWEEN THE RESTRICTION SITES TO INSERT
THE MUC1(16) EPITOPE AT VARIOUS LOCATIONS

```
      G V T S A P D T R P A P G S T A
      GGTGTTACTTCTGCTCCTGATACTAGACCTGCTCCTGGTTCTACTGCT
      CCACAATGAAGACGACCCTATGATCTGGACGAGGACCAAGATGACGA
      ↙                               ↘
          ↓                           ↓
      GATCC                         TCTAAGACTGCTGTT
      G                               AGATTCTGACGACAA

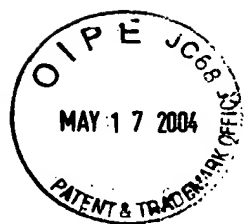
      GATCCTCT                     AAGACTGCTGTT
      GAGA                         TTCTGACGACAA

      GATCCTCTAAG                 ACTGCTGTT
      GAGATTC                     TGACGACAA

      GATCCTCTAAGACT             GCTGTT
      GAGATTCTGA                 CGACAA

      GATCCTCTAAGACTGCT         GTT
      GAGATTCTGACGA             CAA
```

FIG. 11B



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LTSV : NI---YAPARLTIAA-ANSSINIASVGTLYATYEVEL
SBMV : NIGNILVPARLVIAIEGGSSKTAVNTGRLYASYTIRL
SMV : NIATDLVPARLVIALLDGSSSTAVAAGRIYASYTIQM

#####=====#####

β H loop β I

FIG. 12



LIPMAN-PEARSON PROTEIN ALIGNMENT

KTUPLE: 2; GAP PENALTY: 4; GAP LENGTH PENALTY: 12

SEQ1(1>389)	SEQ2(1>340)	SIMILARITY	GAP	GAP	CONSENSUS
tbsvtbs.PRO	rcnmvdia.PRO	INDEX	NUMBER	LENGTH	LENGTH
(64>387)	(8>338)	26.9	4	7	331

70 80 90 100 110 120
KKQOMINHVGGTGGAIMAPVAVTRQLVGSKPKFTGRTSGSVTVTHREYLSQVNNSTGFQV
K.:Q. :. : T. :. : .VA: . . . : . : H : : V .S. :.
KSKQRSQPRNRTPTNTSVKTVAIKQIITVNPFPKARGILHTQLVMSVVGSVQMRT
10 20 30 40 50 60
130 140 150 160 170 180
NGGIVGNLLQLNPLNGTLFSWLPASNFQYTFNSVVLHYVPLCSTTEVGRVAIYFDKD
N.G :. : LNP N :LF: L: A:N:D Y :. : L:YVPL :. : GRVA: .D D
NNGKSNQRFRLNPSNPALFPTLAYEANYDMYRLKKLTLRYVPLVTVQNSGRVAMIWDPD
70 80 90 100 110 120
190 200 210 220 230 240
SEDPEPADRVELANYSVLKETAPWAEAMLRVPTDKIKRFCDSDSSTSDHKLIDLGQLGIAT
S:D:.P..R E:..YS .TA ... L :P:D: RF .D::T D:KL:D:GQL :.T
SQDSAPQSRQEISAYSRSVSTAVYEKCSLTIPADNQWRFVADNTTVDRKLVDFGQLLFVT
130 140 150 160 170 180
250 260 270 280 290 300
YGGAGTNAVGDIFISYSVTLYFPQPTNTLLSTRRLDLAALVTASGPGYLLVSR---TAT
.:G:.. :GDIF:..V.: PQPT:.. : :DL:G:L: .GP:YL: : T:..
HSGSDGIETGDIFLDCEVEFKGPQPTASIVQKTVIDLGGTLTSFEGPSYLMPPDAFITSS
190 200 210 220 230 240
310 320 330 340 350
VLTMTFRATGTFVISGTYRCLTATTLGLAG--GVNVNSITVVDNIG-TDSAFFINCTVSN
.: :GT:.. : C T:.. :G :. : : : : :S F:..V :
SFGLFVDVAGTYLLTLVVTCTTGSVTVGGNSTLVGDGRAAYGSSNYIASIVFTSSGVLS
250 260 270 280 290 300
360 370 380
LPSVVTFT-STGITSATVHCVRATRQNDVSL
.: V F: S:G:.. : R :. N. L
TTPSVQFSGSSGVSRVQMNICRCKQGNTFIL
310 320 330

FIG. 14

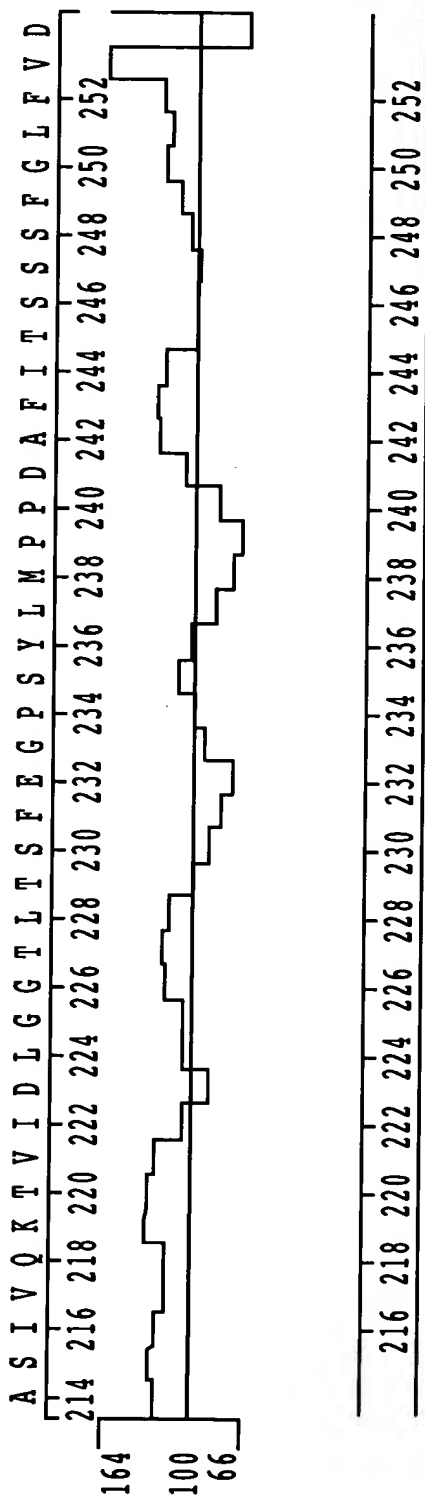


FIG. 15



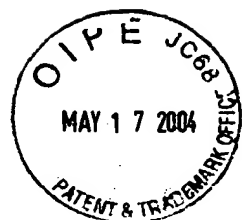
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	220	230	240
AA	ASIVQKYVIDLG GTLTSFEGPSYLMPP		
PHD sec	HHHHHEEEE	EEEE	EEEE
Rel sec	145432244525515625586487624		
detail :			
prH sec	46665532111110000000000000		
prE sec	101123456632246752212688753		
prL sec	422221112246642237787311246		
subset : SUB sec	..H.....E.LL.EE.LLLL.EEE..		

ABBREVIATIONS:

AA: AMINO ACID SEQUENCE
H: HELIX
E: EXTENDED (SHEET)
BLANK: OTHER (LOOP)
PHD: PROFILE NETWORK PREDICTION HEIDELBERG
Rel: RELIABILITY INDEX OF PREDICTION (0-9)
prH: PROBABILITY FOR ASSIGNING HELIX
prE: PROBABILITY FOR ASSIGNING STRAND
prL: PROBABILITY FOR ASSIGNING LOOP
SUB: A SUBSET OF THE PREDICTION, FOR ALL RESIDUES
WITH AN AVERAGE EXPECTED ACCURACY OF >82%

FIG. 16



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SEQUENCE OF RCNMV COAT PROTEIN SPANNING THE POTENTIAL INSERTION SITE WITH
INTRODUCED BASE CHANGES AND NEW RESTRICTION SITES: (SEQUENCE STARTS AT nt 3070)

```

S I V Q K T V I D L G G T L T S F
AGCATCGTACAGAAACTGTAATTGATCTCGGTGGGACACTCACTTCTTTC
      ↓      ↓
    GTGCAC
    Apal I
      ↓      ↓
    GTTAAC
    Hpal

```

FIG. 17A

SERIES OF SEQUENCES TO BE INSERTED BETWEEN THE RESTRICTION SITES TO INSERT
THE MUC1(16) EPITOPE AT VARIOUS LOCATIONS

```

G V T S A P D T R P A P G S T A
GGTGTTACTTCTGCTCCTGATACTAGACCTGCTCCTGGTTCTACTGCT
CCACAATGAAGACGACCACTATGATCTGGACGAGGACCAAGATGACGA
      ↙               ↘
      GAAAACTGTA
      ACGTCTTTTGACAT
      GAAAACTGTAATT
      ACGTCTTTTGACATTAA
      GAAAACTGTAATTGAT
      ACGTCTTTTGACATTAATA
      GAAAACTGTAATTGATCTC
      ACGTCTTTTGACATTAAGTAGAG
      GAAAACTGTAATTGATCTCGGT
      ACGTCTTTTGACATTAAGTAGAGCCA
      GAAAACTGTAATTGATCTCGGTGGG
      ACGTCTTTTGACATTAAGTAGAGCCACC
      ATTGATCTCGGTGGGACGTT
      TAACTAGAGCCACCCTGCAA
      GATCTCGGTGGGACGTT
      CTAGAGCCACCCTGCAA
      CTCGGTGGGACGTT
      GAGCCACCCTGCAA
      GGTGGGACGTT
      CCACCCTGCAA
      GGGACGTT
      CCCTGCAA
      ACGTT
      TGCAA

```

FIG. 17B



NUCLEOTIDE AND AMINO-ACID SEQUENCE OF THE C-TERMINAL REGION OF THE COAT PROTEIN OF TRV:

1125 S T P A S G S G A T P P P A S G G A V R P N P *
CGTCGACTCCGGCCCTCGGGGGAAGTGGTGCAACACCCTCCTCGGAGTGGGGTCTGTGCTCCTAATCCTTGATGTCGTCAAAATCAAAACCTTTAAGGACCTT1230
↑ Sal I ↑ PpuM I

FIG. 18A

SERIES OF SEQUENCES TO BE INSERTED BETWEEN THE Sal I AND PpuM I RESTRICTION SITES TO CREATE C-TERMINAL DELETIONS:

S T P A S G S G A T P P P A S G G A *
TCGACTCCGGCCCTCGGGGGAAGTGGTGCAACACCCTCCTCGGAGTGGGGTCTGTGATGTCGTCAAAATCAAAACCTTTAAGG
GAGGCCGAGCCCCCTTCACCACGTTGTGGTGAGGACGCTCACCCTCAGGAACTACAGCAGTTTAGTTTGGAAATTCCTCG

S T P A S G S G A T P P P *
TCGACTCCGGCCCTCGGGGGAAGTGGTGCAACACCCTCCTTGATGTCGTCAAAATCAAAACCTTTAAGG
GAGGCCGAGCCCCCTTCACCACGTTGTGGTGAGGAACTACAGCAGTTTAGTTTGGAAATTCCTCG

S T P A S G S G *
TCGACTCCGGCCCTCGGGGGAAGTGGTGATGTCGTCAAAATCAAAACCTTTAAGG
GAGGCCGAGCCCCCTTCACCAACTACAGCAGTTTAGTTTGGAAATTCCTCG

S T P A *
TCGACTCCGGCCCTGATGTCGTCAAAATCAAAACCTTTAAGG
GAGGCCGAGCTACAGCAGTTTAGTTTGGAAATTCCTCG

S T *
TCGACTGATGTCGTCAAAATCAAAACCTTTAAGG
GAACTACAGCAGTTTAGTTTGGAAATTCCTCG

FIG. 18B